DETAILED ACTION

Status of the Application

The remarks and amendments filed on August 24th, 2010 are acknowledged. Claims 24-31 are amended, canceled, withdrawn, included in the prosecution.

Response to arguments

Withdrawn Rejections

Receipt and consideration of Applicants' amended claim set and remarks filed on August 24th 2010 is acknowledged. Rejections and objections not reiterated from previous office actions are hereby withdrawn. The following rejections or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

In regards to the specific rejection of claims 24-29 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements being: Rhenium-188. Applicant argues that the kits do not need to contain rhenium-188, and thus the preamble of the claim is merely an intended use of the kit. For this reason the 112 2nd rejection has been withdrawn and the preamble is being interpreted to be non-limiting.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Jia, W., et al., (J. of Radioanal. and Nuclear Cehmistry, 1995) provided in the IDS.

This rejection is MAINTAINED for the reasons of record set forth in the office action mailed on May 24th 2010 and for the reasons set forth below. Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues: "Claim 30 is not anticipated by *Jia et al.*"

In response to this argument, applicant ha added the limitation of "in a ready-to-use solution" to the claim. This term is indefinite, new matter, and even with this addition the final particles of Jia are labeled Rhenium particles in saline (a ready to use form) which still anticipates instant claims 30-31.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jia, W., et al., (J. of Radioanal. and Nuclear Cehmistry, 1995) provided in the IDS in view of Sialerova, E., et al., (Applied Radiation, and Isotopes, 2003) provided in the IDS, and Rhodes U.S. Patent 5,078,985.

This rejection is MAINTAINED for the reasons of record set forth in the office action mailed on May 24th 2010 and for the reasons set forth below. Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues: "In contrast to the present invention, in *Jia et al.* the Re labeled product contains no supernatant and no added buffer substance; the supernatant has been removed and replaced with DI water or saline solution."

In response to this argument, applicant ha added the limitation of "in a ready-to-use solution" to the claim. This term is indefinite, new matter, and even with this addition the final particles of Jia are labeled Rhenium particles in saline (a ready to use form). Furthermore the applicant is arguing limitations not found in the claims such as the presence of supernatant or buffer substances.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 recites the term "ready to use solution". What is a ready to use solution? If I am do anything with the solution it was ready to be used for that purpose. This term renders the claim indefinite.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Instant claim 24 now recites the use of 0.5 mol to 2 mol complexing agent, however the specification states: “For each application to the patient the kit contains preferably **0.5 to 2 mol**, in particular preferably 1 mol, of the complexing agent stabilizing the tin-II salt **per mol tin-II salt**. This corresponds to a quantity of 5 mg to 20 mg gentisic acid.” The molecular weight of 2,5-dihydroxybenzoic acid has a molecular weight of 154.12, 5 mg to 20 mg of gentisic acid is nowhere near 0.5 to 2 mol. Furthermore elsewhere in the application it is stated that “the complexing agent for stabilizing the tin-II salt has in solution preferably a concentration of 50 mmol/l to 30 mmol/l, particularly preferred 20 20 mmol/l” it appears that applicant has reconstrued their own specification away from its own teachings and is relying upon this

for patentability, however the majority of the evidence points towards the range described in the specification as being mmol quantities of the chelating compound and not mol quantities. The passage which applicant has copied does not teach 0.5 to 2 mol of the chelating agent, if fact it teaches a ratio of 0.5 to 2 mol of complexing agent to 1 mole tin-II salt. Thus the specification teaches a range of 0.01 mmol to 0.2 mmol of the chelating reagent, not 0.5 mol to 2 mol of the chelating reagent.

Claims 30-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no recitation of a "ready-to-use solution" anywhere in the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wunderlich, (Applied Radiation and Isotope, 2000) in view of Crockford, U.S. Patent 4,424,200 and Rhodes, U.S. Patent 5,078,985.

Wunderlich teaches a glass vial containing 3 mg of gentisic acid also named 2,5-dihydroxybenzoic acid (20 umol), 3.9 mg of $SnCl_2$-$2H_2O$ (17 umol, very close to the claimed 0.020 mmol) and then adding 2.5 mg HSA microspheres from a ^{99m}Tc labeling kit to the vial. (See page 64 paragraph 6.) The HSA microspheres have a mean particle diameter of 25 um. (See page 64, paragraph 2, and figure 1.) The reagents used read on the reagents of the instant kit. The particles formed read on the particles claimed in instant claims 30-31.

The references do not specifically teach adding the ingredients in the amounts as claimed by Applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results, such as complete reduction of a radioactive ion onto the surface of a protein. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Applicant's invention. Furthermore the instantly claimed amounts are the result of scaling up the quantities of the reactants used. It has been previously determined that the "mere scaling up of a prior art process capable of being scaled up, if such were the case, would not establish patentability in a claim to an old process so scaled." See *In re Rinehart*, 531 F.2d at 1053, 189 USPQ at 148. A direct doubling of the ingredients to make enough reagent for 6 rats rather than the 3 disclosed would read on the instantly claimed range of compounds.

Wunderlich does not teach adding a buffering composition of sodium potasiium tartrate to the kit of stannous chloride, gentisic acid, and HAS microspheres.

Crockford teaches kits for labeling proteins comprising a package containing a source of stannous ion and a buffering composition containing a alkali metal tartrate with a pH of 4.5 to 8.5 and an gentisate (2,5-dihydroxybenzoic acid). (See claims 16-

17.) Crockford teaches specific examples using a mixture 20 mL of 10 mM sodium potassium tartrate (0.2 mmol) and 0.2 mL of stannous chloride (0.1 mmol). Crockford teaches that the buffering composition does not interfere with the tin reduction of the radioactive metal and that after mixing the tin solution with the buffer solution the pH is between 4.5 and 8.5. (See column 3, lines 15-30.) Crockford teaches that the buffer can be mixed with the stannous chloride or stored in a separate container as instantly claimed. (See column 4, lines 25-30.) Crockford also teaches that gentisic acid provides an antioxidant effect and protects the metal radionuclide metal label against degradation. (See example III.)

It would have been prima facie obvious to add a common buffering agent (sodium potassium tartrate/biphthalate) which was known to be useful for buffering protein compositions radiolabeled with radioactive metals by tin reduction into a kit for radiolabeling protein microspheres by tin reduction in order to form a kit in which the buffering agent would not react and interfere with the radiolabeling process. The skilled artisan would have predicted that the addition of the kit reagent of sodium potassium tartrate to the kit disclosed by Wunderlich would have functioned as both kits use the same materials of gentisic acid, tin-II chloride, and albumin to form radioactively labeled protein substrates.

Wunderlich and Crockford do not teach that both technetium and rhenium are equivalent radioactive metals and would be reduced by similar methods.

Rhodes teaches methods of reducing both rhenium and technetium. The methods use the same materials of gentisic acid, tin-II chloride, and sodium potassium tartate for the protein reducing solution. (See example II.)

It would have been prima facie obvious to one of ordinary skill in the art to combine kits drawn to radiolabeling proteins with either rhenium or technetium with gentisic acid, tin-II chloride, and sodium potassium tartate as Rhodes teaches that usch methods are applicable to either metal radionuclide.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LANCE RIDER whose telephone number is (571)270-1337. The examiner can normally be reached on M-F 11-12 and 1-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LANCE RIDER/
Examiner, Art Unit 1618

/Jake M. Vu/
Primary Examiner, Art Unit 1618